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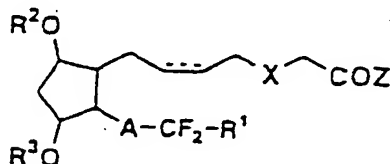
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(54) Difluoroprostaglandin derivatives and their use

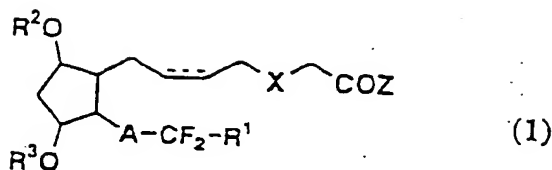
(57) A fluorine-containing prostaglandin derivative of the formula (1) or a salt thereof, and a medicine containing it, particularly, as a preventive or therapeutic medicine for an eye disease:



(1)

wherein A is a vinylene group or the like, R¹ is an aryloxyalkyl group or the like, R² and R³ are hydrogen atoms or the like, and Z is OR⁴, therein OR⁴ is a hydrogen atom or an alkyl group or the like.

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10 wherein A is an ethylene group, a vinylene group, an ethynylene group, $-OCH_2-$ or $-SCH_2-$,

R^1 is a substituted or unsubstituted C_{3-8} alkyl group, a substituted or unsubstituted C_{3-8} alkenyl group, a substituted or unsubstituted C_{3-8} alkynyl group, a substituted or unsubstituted C_{3-8} cycloalkyl group, a substituted or unsubstituted aralkyl group or a substituted or unsubstituted aryloxyalkyl group,
 15 each of R^2 and R^3 which are independent of each other, is a hydrogen atom or an acyl group, or forms a single bond together with Z,

X is $-CH_2-$, $-O-$ or $-S-$,

Z is $-OR^4$, $-NHCOR^5$, $-NHCO_2R^6$ or $-SR^7$, or forms a single bond together with R^2 or R^3 ,

20 each of R^4 , R^5 , R^6 and R^7 which are independent of one another, is a hydrogen atom, an alkyl group, an alkenyl group, an alkynyl group, a cycloalkyl group, an aryl group or an aralkyl group,
 and a dual line consisting of solid and broken lines is a single bond, a cis-double bond or a trans-double bond.

2. The compound according to Claim 1, wherein A is an ethylene group or a vinylene group.

25 3. The compound according to Claim 1 or 2, wherein X is $-CH_2-$.

4. The compound according to any one of Claims 1 to 3, wherein Z is $-OR^4$.

5. The compound according to any one of Claims 1 to 4, wherein R^1 is a substituted or unsubstituted aryloxyalkyl group.
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6. The compound according to Claim 5, wherein R^1 is a phenoxyethyl group, a 3,5-dichlorophenoxyethyl group or a 3-chlorophenoxyethyl group.

35 7. 16-Phenoxy-15-deoxy-15,15-difluoro-17,18,19,20-tetranorprostaglandin $F_{2\alpha}$, 16-(3-chlorophenoxy)-15-deoxy-15,15-difluoro-17,18,19,20-tetranorprostaglandin $F_{2\alpha}$, 16-phenoxy-15-deoxy-15,15-difluoro-13,14-dihydro-17,18,19,20-tetranorprostaglandin $F_{2\alpha}$ or an alkyl ester or a salt thereof.

8. A medicine containing the compound according to any one of Claims 1 to 7 as an active ingredient.
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9. A preventive or therapeutic medicine for an eye disease containing the compound according to any one of Claims 1 to 7 as an active ingredient.

45 10. The medicine according to Claim 9, wherein the eye disease is glaucoma or ocular hypertension.



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EUROPEAN SEARCH REPORT

Application Number
EP 97 12 2702

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THE HAGUE	22 April 1999	BERTE, M	
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

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**ANNEX TO THE EUROPEAN SEARCH REPORT
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This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82